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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/988,792 | 11/20/2001 | Andrzej W. Lipkowski | 18475-025 (NEMC-6) | 9119 |

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| EXAMINER |
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | 6 |

DATE MAILED: 06/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/988,792 | LIPKOWSKI ET AL. | |
| | Examiner | Art Unit | |
| | Vanessa L. Ford | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *15-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. Applicant's response to the Restriction requirement filed in Paper No. 4 filed on 22 February 2002 is acknowledged. Applicant's election of Group I, claims 1-14 and 24 is acknowledged. Claims 15-23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being to a non-elected invention.

### *Specification Objections*

2. The specification is objected because of the use of worldwide web addresses on page 11, line 28. The worldwide web address can be readily changed and therefore, may not be available to the public.

### *Claim Objections*

3. Claim 11 is objected to because of the following informalities: What appears to be a typographical error: "Bacteriim" should be changed to "Bacterium".

### *Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-14 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a written description rejection.*

The specification broadly describes as a part of the invention polypeptides consisting of the polypeptides SEQ ID Nos: 1, 2, 12 and 13. The specification teaches that the sequences (i.e. SEQ ID Nos: 1, and 6-11) of native substance P have been reported in various organisms, which is disclosed in Table 1 (pages 11-12). Applicant has broadly described the invention as embracing any substitution, insertion or deletion change of amino acids throughout the length of the polypeptide sequence. Variants SEQ ID Nos: 1-2, 12 and 13 correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a variant degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 U.S.C. 112, first, paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptide regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NOs: 1 and 2 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

5. Claims 1-14 and 24 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID Nos: 1 and 2 does not reasonably provide enablement for the full breadth of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-14 and 24 are directed to isolated polypeptides selected from the groups consisting of SEQ ID NOs: 1, 2, 12 and 13 and variants thereof.

The specification is enabling only for the polypeptides of SEQ ID NOs: 1 and 2 as disclosed in the specification. The specification states that "Substance P peptides are at least 50% identical to the sequences of SEQ ID No: 1 or 2." The specification also teaches that the substance P peptides art at least 75%, 85%, 95% and 99% identical to the SEQ ID Nos. 1 or 2". The specification further states that " a conservative substitution of one amino acid for another is a replacement by an amino acid having similar chemical functional side group, e.g. replacement by another amino acid by another positively charged amino acid or replacement of a hydrophobic amino acid by another hydrophobic amino acid" (page 7). There is no guidance provided as to which amino acids can be added, deleted or substituted and the polypeptide would retain its biological function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of the polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the polypeptide's structure relates to function. However, the problem of the prediction of polypeptide structure from

mere sequence data of a single polypeptide and in turn utilizing predicted structural determinations to ascertain functional aspects of the polypeptide and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple substitutions or multiple modifications of other types and the positions within the polypeptide's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any polypeptide and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modifications, e.g., multiple substitutions. The sequence of some polypeptides is highly conserved and one skilled in the art would not expect tolerance to any amino acid modification in such polypeptides.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or

guidance is presented in the specification with respect to selecting other antigens having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use polypeptides that are variants of SEQ ID NOs: 1,2 and SEQ ID Nos: 12 and 13 in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation to make and use these polypeptides is undue.

6. Claims 1-11 are rejected under 35 U.S.C. 102(b) as anticipated by Folkers et al, *(U.S. Patent No. 4,481,139, published November 6, 1984).*

Claims 1-11 are drawn to an antibacterial composition comprising a substance P peptide.

Folkers et al teach compositions that comprise antagonists of substance P that are useful to elucidate some biological mechanisms of substance P and treat inflammatory responses in the eye for medical practice in opthtalmology. The amino acid sequence of the Folkers et al (see the Abstract) is the same as the claimed invention (SEQ ID NO:1).

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See

In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

7. Claims 1-4, 7 and 10 are rejected under 35 U.S.C. 102(b) as anticipated by Rosengurt et al, *(WO 88/07551*, published October 6, 1988).

Claims 1-4, 7 and 10 are drawn to an antibacterial composition comprising a substance P peptide.

Rosengurt et al teach a composition comprising the substance P peptide. Rosengurt et al teach that composition of their invention has the same amino acid sequence as SEQ ID NO: 1 (page 3). Rosengurt et al also teach a commercially available composition that is a structural variant of Substance P that has the amino acid sequence of SEQ ID No: 2 (page 4). Rosengurt et al teach that the antagonists or antibodies of their invention may be formulated with pharmaceutically acceptable carriers or diluents (page 6). The recitation of an "antimicrobial composition" is being viewed as a limitation of intended use. The composition of Rosengurt, et al is the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 1-10 are rejected under 35 U.S.C. 102(b) as anticipated by Horig *(WO 83/01251, published April 14, 1983).*

Claims 1-10 are drawn to an antibacterial composition comprising a substance P peptide.

Horig teaches a composition comprising peptides or the pharmaceutically acceptable salts and agents and/or conventional pharmaceutical adjuvants (see the Abstract). The recitation of an "antimicrobial composition" is being viewed as a limitation of intended use. Horig teaches a composition that comprises the amino acid sequence of SEQ ID Nos: 1, 2 and 12. The composition of Horig is the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 1-11 are rejected under 35 U.S.C. 102(b) as anticipated by De Simone et al *(Journal of Clinical Lab Anal.,1989, 3(6):345-349).*

Claims 1-11 are drawn to an antibacterial composition comprising a substance P peptide.

De Simone et al teach the effects of substance P on *Salmonella minnesota*. De Simmone et al teach that substance P inhibits the binding of blood lymphocytes and bound-bacteria/lymphocytes. De Simone et al teach that substance is able to hamper the bacterial cytoadherence to T cells. De Simone et al discloses that substance P is involved in the mechanism of host protection against invading microorganisms (see the abstract). The recitation of an "antimicrobial composition" is being viewed as a limitation of intended use. The amino acid sequences of substance P would be inherent in the teaching of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

10. Claims 1-11 are rejected under 35 U.S.C. 102(b) as anticipated by Schroeder et al *(Acta virologica, September 1986, 30(5), p. 432-335).*

Claims 1-11 are drawn to an antibacterial composition comprising a substance P peptide.

Schroeder et al teach that substance P inhibits measles virus replication in cell culture and partially blocks viral infection activity assayed in the haemolysis system (see the Abstract). The recitation of an "antimicrobial composition" is being viewed as a limitation of intended use. The amino acid sequences of substance P would be inherent in the teaching of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Claims 1- 7, 9 and 24 are rejected under 35 U.S.C. 102(b) as anticipated by Visser et al *(WO 92/18536, published October 29, 1992).*

Claims 1-7, 9 and 24 are drawn to an antibacterial composition comprising a substance P peptide.

Visser et al teach compositions comprising substance P (page 1 and claims 7-9, page 15). Visser et al also disclose kits containing substance P (page 7 and claims 14-18, pages 16-17). The recitation of an "antimicrobial composition" is being viewed as a

limitation of intended use. The claimed SEQ ID NO: 1 is the same as the amino acid sequence disclosed in the prior art (page 4, line 23). The composition and kit of the Visser et al is the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition and kit with the composition and kit of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition and kit of the prior art does not possess the same material structural and functional characteristics of the claimed composition and kit). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

12. Claims 1-2, 7 and 11-14 are rejected under 35 U.S.C. 102(e) as anticipated by De La Charriere et al *(U.S, Patent No. 6,203,803, filed June 24, 1997).*

Claims 1-2, 7 and 11-14 are drawn to an antibacterial composition comprising a substance P peptide further comprising a second antimicrobial agent.

De La Charriere et al teach a substance P antagnoist in a cosmetic composition used to treat sensitive skin (see the Abstract). De La Charriere et al teach that the compositions of their invention comprise antibacterial agents such as erythromycin belong to the group of tetracyclines and antifungal agents such as econazole belong to the group of imidazoles (column 6). The amino acid sequence would be inherent in the teachings of the prior. The composition of the De La Charriere et al is the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition and kit of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

***Pertinent Prior Art***

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Riegler et al, The American Physiological Society, 1999).*

***Status of Claims***

14. No claims are allowed.

***Conclusion***

15. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
May 31, 2002

JAMES O. WILSON
PRIMARY EXAMINER
GROUP 1600